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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,869	11/26/2003	Kevin R. Stone	CROL-156 (56290-103)	8648

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EXAMINER	
MAYER, SUZANNE MARIE	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,869	STONE, KEVIN R.	
	Examiner	Art Unit	
	Suzanne M. Mayer, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *10-23* is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-23 are pending in this application.

Withdrawn Claim Objections/Rejections

2. Rejection of claims 1-23 under 35 U.S.C. § 102(b) and 103(a) are hereby withdrawn.

New Claim Rejections

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuberasampath et al. Kuberasampath et al. teach type I bone matrix collagen that is either xenogeneic or allogenic which can be implanted in a mammalian host (see Claim 1). The term implantable is defined as either surgical introduction, topical applications OR introduction by injection (see column 4, lines 46-49). In addition, the bone matrix type I collagen is deglycosylated by the treatment with hydrogen fluoride, which is a known deglycosylating agent (see column 10, lines 9-17; and claims 1 and 28). Thus all

of the limitations of the claims have been met when one considers that human are of course mammals.

5. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention. Collagen Corporation has been selling Zyderm (I and II) and Zyplast collagen since 1981. The collagens are created as an injectable form of bovine collagen that has been approved by the FDA for use in humans, which obviates it as being xenogeneic. It is also substantially non-immunogenic as only 3% of the population is allergic to bovine collagen. Thus the limitations of the claims as recited have been met.

6. Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Daniels et al. Daniels et al. teach injectable collagen that is xenogeneic which is implantable into humans (see claims 1 and 5). The collagen can be sterilized by several different techniques including by dialysis, irradiation or chemical treatment (see column 3, lines 23-25). Thus the limitations of the claims have been met.

Claim Rejections - 35 USC § 103

7. Claims 1,3, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. in view of Odland et al.

The method and composition of Daniels et al is described in detail in Section 6 of this Office action. However, Daniels et al. do not teach the use of e-beam ionization radiation in a dose approximately equal to 17.8 kGy for the sterilization of collagen containing soft tissue xenografts.

Odland teaches a method for sterilizing biological tissues using E-beam radiation (electron beam radiation) by using accelerating electron systems such as Van de Graaf generators, Dynamitrons, or linear particle accelerators (see Col. 2, lines 52-55).

A person of ordinary skill in the art at the time the invention was made would have been motivated to use the method of e-beam sterilization in place of the silent nature of the specific irradiation technique to be employed by Daniels et al. because Odland teaches that the integrity of collagen containing material is maintained by this sterilization method and because it is much quicker to use this sterilization technique.

Typically the biological tissue is subjected to one-sided exposure to the electron beam, until a sterilizing dose of radiation is absorbed. Odland teaches the use of the approximately 25-28 kGy in his preferred sterilization method as this is in accordance with what the FDA requires for sterilization of medical products (see col. 6, lines 1-9). However, he further points out that effective sterilization doses may be easily determined using conventional microbiological techniques, such as including suitable biological indicators in the radiation batch, or can the dose can be determined using radiochromic dye films (see col. 6, lines 29-36). Therefore, would be obvious to adapt the dose to the specific biological tissue, therefore if 17.8 kGy is the optimum dose it would be obvious to use this amount. Furthermore, Odland shows that the integrity of collagen in a biological tissue (porcine aortic leaflets) is maintained after sterilization with 25 kGy of E-beam radiation (see Col. 9, Example 2, and Table 1). Finally, Odland teaches that the use of E-beam radiation for sterilization is much quicker than with

gamma radiation because gamma radiation requires a low dose rate in combination with a high exposure periods (see column 3, lines 7-13).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the method of E-beam radiation as taught by Odland and apply it with the methods and teaching of Daniels et al. who are silent on the exact and specific teaching of which irradiating techniques can be employed in their methods.

8. Claims 1, 3 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daniels et al. in view of Spira et al.

The method and composition of Daniels et al is described in detail in Section 6 of this Office action. However, Daniels et al. do not teach the use of 0.2-3.0 MegaRad gamma radiation to sterilize the injectable collagen.

Spira et al. teach the preparation of an allogeneic collagen for injection into humans. The also teach that their optimum sterilization dose was 0.25 MegaRad of gamma radiation. They further teach that at this level, even AIDS viral samples become noninfectious, thus implying it is a sufficient level to sterilize (see p. 95, 1st column last line through to 2nd column, 1st paragraph.)

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the method of gamma radiation in order to sterilize collagen and to use gamma radiation as an option in place of the silent nature of the specific irradiation technique to be employed by Daniels et al. One would be motivated and expect success in doing so because Spira et al. teach that 0.25

MegaRads is sufficient in sterilizing their collagen, and because at this level it is even sufficient to reduce the viral effects of AIDS samples.

Conclusion

8. Claims 1-9 are rejected. Claims 10-23 are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Mayer, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached on Monday to Friday, 8.30am to 5.00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SMM
10 June 2005

ROBERT A. WAX
PRIMARY EXAMINER
Art Unit 1653